BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
James T. Kadonaga	Associate Professor

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Massachusetts Institute of Technology	S.B.	1980	Chemistry
Harvard University	A.M.	1982	Chemistry
Harvard University	Ph.D.	1984	Chemistry
University of California, Berkeley	postdoc	1984-88	Biochemistry

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. DO NOT EXCEED TWO PAGES.

Research

1980-84	Graduate Student. Harvard University. Advisor: J. R. Knowles.
1984-88	Postdoctoral Research Fellow. UC Berkeley. Advisor: R. Tjian.
1988-92	Assistant Professor of Biology. University of Calfornia, San Diego.
1992-present	Associate Professor of Biology. University of California, San Diego.

Academic Honors

1980	Alpha Chi Sigma Prize; Massachusetts Institute of Technology
1980	American Institute of Chemists Certificate; Massachusetts Institute of Technology
1983-84	Du Pont Fellow; Harvard University
1984-86	Fellow of the Miller Institute for Basic Research in Science; UC Berkeley
1986-87	Senior Fellow of the American Cancer Society, California Division; UC Berkeley
1987-93	Lucille P. Markey Scholar in Biomedical Sciences
1989-91	Eli Lilly Biochemistry Award
1992-97	Presidential Faculty Fellow Award
1994	Fellow of the American Association for the Advancement of Science

Scientific Activities

1989-present	Co-organizer. Course on "Protein Purification and Characterization." Held annually at Cold Spring Harbor Laboratory.
1990-present	Editorial Board of Protein Expression & Purification.
1992-94	Member of National Science Foundation grant review panel.
1993-95	Editorial Board of Molecular & Cellular Biology.
1994-present	Editorial Board of Genes & Development.
1995	Co-organizer. FASEB Summer Conference on "Chromatin and Transcription."
1996	Co-organizer. FASEB Summer Conference on "Transcriptional Regulation during Cell Growth, Differentiation, and Development."

James T. Kadonaga – Selected Relevant Publications (out of a total of 40)

1. Kadonaga, J. T., and Tjian, R. (1986). Affinity purification of sequence-specific DNA binding proteins. Proc. Natl. Acad. Sci. U.S.A. **83**, 5889-5893.
2. Kadonaga, J. T., Carner, K. R., Masiarz, F. R., and Tjian, R. (1987). Isolation of cDNA encoding transcription factor Sp1 and functional analysis of the DNA binding domain. Cell **51**, 1079-1090.
3. Kadonaga, J. T., Courey, A. J., Ladika, J., and Tjian, R. (1988). Distinct regions of Sp1 modulate DNA binding and transcriptional activation. Science **242**, 1566-1570.
4. Kadonaga, J. T. (1990). Assembly and disassembly of the *Drosophila* RNA polymerase II complex during transcription. J. Biol. Chem. **265**, 2624-2631.
5. Wampler, S. L., Tyree, C. M., and Kadonaga, J. T. (1990). Fractionation of the general RNA polymerase II transcription factors from *Drosophila* embyros. J. Biol. Chem. **265**, 21223-21231.
6. Kerrigan, L. A., Croston, G. E., Lira, L. M., and Kadonaga, J. T. (1991). Sequence-specific transcriptional antirepression of the *Drosophila Krüppel* gene by the GAGA factor. J. Biol. Chem. **266**, 574-582.
7. Kamakaka, R. T., Tyree, C. M., and Kadonaga, J. T. (1991). Accurate and efficient RNA polymerase II transcription with a soluble nuclear fraction derived from *Drosophila* embyros. Proc. Natl. Acad. Sci. USA **88**, 1024-1028.
8. Croston, G. E., Kerrigan, L. A., Lira, L., Marshak, D. R., and Kadonaga, J. T. (1991). Sequence-specific antirepression of histone H1-mediated inhibition of basal RNA polymerase II transcription. Science **251**, 643-649.
9. Croston, G. E., Lira, L. M., and Kadonaga, J. T. (1991). A general method for the purification of H1 histones that are active for repression of basal RNA polymerase II transcription. Protein Expression and Purification **2**, 162-169.
10. Kadonaga, J. T. (1991). Purification of sequence-specific DNA binding proteins by DNA affinity chromatography. Methods Enzymol. **208**, 10-23.
11. Laybourn, P. J., and Kadonaga, J. T. (1991). Role of nucleosomal cores and histone H1 in regulation of transcription by RNA polymerase II. Science **254**, 238-245.
12. Wampler, S. L., and Kadonaga, J. T. (1992). Functional analysis of *Drosophila* transcription factor IIB. Genes & Dev. **6**, 1542-1552.
13. Laybourn, P. J., and Kadonaga, J. T. (1992). Threshold phenomena and long-distance activation of transcription by RNA polymerase II. Science **257**, 1682-1685.
14. Croston, G. E., Laybourn, P. J., Paranjape, S. M., and Kadonaga, J. T. (1992). Mechanism of transcriptional antirepression by GAL4-VP16. Genes & Dev. **6**, 2270-2281.
15. Kerrigan, L. A., and Kadonaga, J. T. (1992). Periodic binding of individual core histones to DNA: inadvertent purification of the core histone H2B as a putative enhancer-binding factor. Nucleic Acids Res. **20**, 6673-6680.
16. Croston, G. E., and Kadonaga, J. T. (1993). Role of chromatin structure in the regulation of transcription by RNA polymerase II. Curr. Opin. Cell Biol. **5**, 417-423.
17. Kamakaka, R. T., and Kadonaga, J. T. (1993). Biochemical analysis of the role of chromatin structure in the regulation of transcription by RNA polymerase II. Cold Spring Harbor Symp. Quant. Biol. **58**, 205-212.
18. Tyree, C. M., George, C. P., DeVito, L. M., Wampler, S. L., Dahmus, M. E., Zawel, L., and Kadonaga, J. T. (1993). Identification of minimal set of proteins that is sufficient for accurate initiation of transcription by RNA polymerase II. Genes & Dev. **7**, 1254-1265.
19. Kamakaka, R. T., Bulger, M., and Kadonaga, J. T. (1993). Potentiation of RNA polymerase II transcription by Gal4-VP16 during but not after DNA replication and chromatin assembly. Genes & Dev. **7**, 1779-1795.
20. Paranjape, S. M., Kamakaka, R. T., and Kadonaga, J. T. (1994). Role of chromatin structure in the regulation of transcription by RNA polymerase II. Annu. Rev. Biochem. **63**, 265-297.

OTHER SUPPORT

I. JAMES T. KADONAGA -- Currently Active Support

A. Council for Tobacco Research

(a). Council for Tobacco Research, 900 Third Avenue, New York, NY 10022. Grant Number: 3171. PI: James T. Kadonaga. Title: "Mechanisms of Gene Activation in Eukaryotes."
(b). Principal investigator: 15% effort on project.
(c). From 01/01/92 through 12/31/94. Direct costs for entire project: $225,330
(d). Annual direct costs: 01/01/94 through 12/31/94: 78,041
(e). Specific Aims
I. Assembly and characterization of higher order chromatin structures
A. Attempt to reconstitute the 30 nm chromatin filament in vitro with a new Drosophila S-100 extract.
B. Identify and purify factors in Drosophila embryos that interact with scaffold (matrix) attachment regions.
(f). No overlap.
(g). No adjustments.

B. NIH GM41249

(a). Public Health Service. National Institute of General Medical Sciences.
Grant Number: 2 R01 GM41249-06. PI: James T. Kadonaga
Title: "Mechanisms of Transcriptional Regulation in Eukaryotes."
(b). 24% effort on project.
(c). From 12/01/88 through 11/30/97. Estimated direct costs of entire project: $597,343
(d). Annual direct costs:

12/01/93 through 11/30/94	140,785
12/01/94 through 11/30/95	146,336 (recommended support)
12/01/95 through 11/30/96	152,109 (recommended support)
12/01/96 through 11/30/97	158,113 (recommended support)

(e). Specific Aims
A. Identification and characterization of factors that are required for basal transcription in addition to TFIIB, TBP, TFIIF30, and polymerase
1. Examination of fractions from the HeLa transcription system.
2. Identification and characterization of factors from the Drosophila transcription system.
3. Investigation of the transcriptional requirement for negatively supercoiled DNA.
4. Study of the function of TFIIE.
B. Examination of the molecular basis for distinct transcriptional properties of different promoters
1. Perform in vitro transcription and gel shift analyses with a systematic series of minimal promoters and promoter hybrids to identify key cis-acting elements that are responsible for differences in the mechanisms of basal transcription.
2. Investigate the protein factors that are responsible for the promoter-specific effects that have been observed.
C. Kinetics and mechanism of transcription with a purified transcription system
1. Determine the relative rates of assembly of the basal transcription factors into a functional transcription complex.
2. Investigate the rates of assembly of the factors with different promoters as well as with wild-type and mutant variants of selected promoters.
3. Examine the kinetics of the transcription reaction with wild-type and mutant variants of the basal transcription factors, such as TFIIB and TBP.

D. Analysis of transcriptional activation with the purified transcription system
   1. Examine the ability of factors such as Sp1 and GAL4 derivatives to activate transcription with the purified, reconstituted transcription system. Consider possible requirements for additional factors, such as TBP-associated factors (TAFs), additional basal factors (beyond TFIIB, TBP, TFIIF30, and polymerase), or chromatin-mediated repression of basal transcription.

(f). No overlap.
(g). No modifications.

C. NIH GM46995

(a). Public Health Service. National Institute of General Medical Sciences.
Grant Number: R01 GM46995. PI: James T. Kadonaga.
Title: "Chromatin Structure and Gene Activity."
(b). Principal investigator: 25% effort on project.
(c). From 07/01/92 through 06/30/96. Estimated direct costs of entire project: $545,637
(d). Annual direct costs:

07/01/93 through 06/30/94	140,043
07/01/94 through 06/30/95	145,644 (recommended support)
07/01/95 through 06/30/96	151,469 (recommended support)

(e). Specific Aims
   I. In vitro transcription analysis with chromatin templates reconstituted from purified components.
      1. Reconstitute chromatin templates with purified components and investigate the specific functions of the following components:
         a. core histone octamers (native and modified);
         b. histone H1 (native H1, H1 variants, and modified forms of H1);
         c. HMG proteins (HMG14/17 and HMG1/2 from calf thymus; HMG D from Drosophila).
      2. Examine the generality and mechanistic basis of transcriptional antirepression. Attempt to reconstitute long-range (>1 kb) enhancer function in vitro with the chromatin templates.
   II. Reconstitution and analysis of chromatin possessing physiological nucleosome spacing by using a crude Drosophila embryo S-150 extract.
      1. Determine conditions for reconstitution and purification of chromatin possessing evenly distributed nucleosomes with a physiological repeat length by using a Drosophila embryo S-150 extract.
      2. Investigate the transcriptional properties of chromatin templates reconstituted with the S-150.
      3. Begin to fractionate and to purify components of the Drosophila embryo S-150 extract that mediate chromatin reconstitution. Investigate, in particular, the determinants of nucleosomal spacing.
   III. Analysis of the chromatin structure of the Drosophila knirps gene both in vitro and in vivo.
      1. Perform in vivo and in vitro footprint analyses of the *knirps* proximal promoter and enhancer regions.
      2. Reconstitute the *knirps* transcriptional control region into chromatin, characterize the chromatin, and attempt to identify factors involved in the establishment or dissolution of nucleosome positioning.

(f). No overlap.
(g). No adjustments.

D. Presidential Faculty Fellow Award

(a). National Science Foundation. Grant Number: MCB-9253739. PI: James T. Kadonaga.
Title: Presidential Faculty Fellow Award. This grant is an award from the President that is administered by the National Science Foundation. The award is not associated with the completion of

any particular project. We have been using the funds to carry out studies (such as electron microscopy) that are not supported by the other grants.
(b). Principal investigator: 1% effort on project.
(c). From 08/15/92 through 07/31/97. Total direct costs: 460,800
(d). Annual direct costs: 10/01/93 through 09/30/94: 93,600
(e). There are no Specific Aims associated with the Presidential Faculty Fellow Award. The funds have been (and will be) used to carry out studies involving electron microscopy of chromatin, for which there exists no other grant support.
(f). No overlap.
(g). No adjustments.

II. JAMES T. KADONAGA -- Applications or proposals pending review

A. National Institutes of Health

(a). National Institutes of Health. PI: James T. Kadonaga
Title: "FASEB Summer Research Conference: Chromatin and Transcription"
(b). Principal investigator: 0% effort
(c). From 06/24/95 through 06/29/95. Total direct costs requested: $25,675
(d). N/A
(e). Funds were requested for partial support (44%) for the third FASEB Summer Research Conference on "Chromatin and Transcription," which will be held on June 24-29, 1995 at the Conference Center at Snowmass Village, Colorado. A primary objective of the conference is to bring together researchers who study transcription factors, chromatin structure, and higher-order nuclear organization.
(f). This grant requests funds for partial support of the FASEB meeting (44%).
(g). Because this grant requests partial support, there would be no adjustments. It is extremely unlikely that the NIH will provide more than $5,000 support for this meeting.

B. National Science Foundation

(a). National Science Foundation. PI: James T. Kadonaga
Title: "FASEB Summer Research Conference: Chromatin and Transcription"
(b). Principal investigator: 0% effort
(c). From 06/24/95 through 06/29/95. Total direct costs requested: $25,675
(d). N/A
(e). Funds were requested for partial support (44%) for the third FASEB Summer Research Conference on "Chromatin and Transcription," which will be held on June 24-29, 1995 at the Conference Center at Snowmass Village, Colorado. A primary objective of the conference is to bring together researchers who study transcription factors, chromatin structure, and higher-order nuclear organization.
(f). This grant requests funds for partial support of the FASEB meeting (44%).
(g). Because this grant requests partial support, there would be no adjustments. It is extremely unlikely that the NIH will provide more than $5,000 support for this meeting.